

### **REMARKS**

Claims 1, 2, 4, 8, 9, 11 and 13-17 are pending in this application. No claim amendments have been made herein.

Applicants note with appreciation the Examiner's withdrawal of the 35 U.S.C. § 103 rejections with regard to Cerami et al., RE38,330 in view of EPA 0 458 589.

### **Rejections under 35 U.S.C. §103**

#### **Combinations**

Claims 1, 2, 4, 7, 8, 9, 11 and 13-17 are rejected under 35 U.S.C. §103(a), as being unpatentable over U.S. Patent RE38,330 to Cerami ("Cerami") in view of U.S. Patent 4,540,408 to Lloyd ("Lloyd") or U.S. Patent 5,153,205 to Lotti ("Lotti").

In the Office Action mailed January 11, 2006 ("Office Action"), the Examiner states that Cerami discloses a method of inhibiting and reversing protein ageing by administering to a patient in need thereof an effective amount of a thiazolium compound represented by Formula (I), and that Cerami does not disclose combining a thiazolium compound with a cholinergic agent. See Office Action at pages 3-4. The Examiner further states that Lloyd "teaches that cholinergic agents such as pilocarpine are suitable agents for treating glaucoma and ocular hypertension", and that Lotti "discloses a method of reducing intraocular pressure and treating glaucoma in mammals by topically administering a cholinergic agonist, i.e., pilocarpine and a cholinergic antagonist." Office Action at page 4.

The Examiner states on page 4 of the office action that "it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Cerami et al. to additionally include the administration of a cholinergic agent because one of ordinary skill in the art would reasonably expect the ocular compositions containing an additional cholinergic agent to reduce any ocular hypertension suffered by the patients in Cerami et al."

Applicants respectfully disagree.

Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness with regard to the Cerami and Lotti or Lloyd references. A *prima facie* case of obviousness requires some suggestion or motivation, either in the references themselves or in the

knowledge generally available in the art, to modify the reference or to combine reference teachings. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See also MPEP 706.02(j).

The instant claims relate to reducing intraocular pressure or improving ocular accommodation by administering a combination of a compound of formula I and a cholinergic agent. The compounds can be administered, for example, intravenously or intracamerally.

Cerami relates to thiazolium compositions and methods for inhibiting and reversing nonenzymatic cross-linking (protein aging). *See, e.g.*, Abstract.

Lloyd describes a disposable applicator for placing a pharmacologically active agent in contact with a moist body surface (e.g., the eye). Ophthalmic agents that can be used in the applicator described in Lloyd include anti-glaucoma agents, including cholinergic agents. *See, e.g.*, Abstract and column 4, lines 27-30.

Lotti describes topical administration of a cholinomimetic agent (e.g., pilocarpine) in combination with a cholinergic M<sub>3</sub> receptor antagonist to the eye of a mammal for reducing intraocular pressure. *See, e.g.*, Abstract.

There is no mention of any cholinergic agent in Cerami. Thus, there is no teaching or suggestion in Cerami that would motivate the skilled artisan to produce a combination of the compounds of the invention with a cholinergic agent (administered ocularly, topically, or otherwise) for reducing intraocular pressure or improving ocular accommodation. Reading Cerami, one of ordinary skill in the art would not be motivated to look to Lloyd or Lotti for teaching of compounds to combine with the Cerami compositions.

The fact that references can be modified does not render the resulting combination obvious unless the prior art also suggests the desirability of the combination. (*See* MPEP §2143.01, citing *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990)). In moving from the prior art to the claimed invention, one cannot base a determination of obviousness on what the skilled artisan might try or find obvious to *try*. Rather, the proper test requires determining what the prior art would have led the skilled artisan to *do*. As described above, there is no suggestion in Cerami that would motivate a skilled artisan to modify the compositions described therein. Thus, the mere fact that the Cerami reference *could* be combined with the Lloyd or Lotti references is not sufficient to establish a *prima facie* case of obviousness.

Moreover, an assertion that modifying the Cerami reference would have been within the ordinary skill of the art at the time the claimed invention was made because the cited references were individually known in the art at the time the instant application was filed is also insufficient to establish a *prima facie* case of obviousness without some objective reason to combine the references. (See MPEP §2143.01, citing *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pate. App. & Inter. 1993)). Thus, the mere fact that the Cerami and Lloyd or Lotti references were known in the art individually at the time the instant application was filed does not render the claimed invention obvious, as there is no teaching or suggestion in the Cerami reference that would motivate one of ordinary skill in the art to modify the compounds and methods described therein. Therefore, Applicants respectfully request withdrawal of this rejection.

#### Counterion

The Examiner states that it “would have been obvious to one of ordinary skill in the art at the time the invention was made to administer 3-(2-phenyl-2-oxoethyl)-4,5-dimethyl-thiazolium chloride because, in view of Cerami et al.’s teaching, one of ordinary skill in the art would reasonably expect the chloride compound to be effective in treating lens proteins susceptible to aging.” Office Action at page 4.

Cerami relates to thiazolium compositions and methods for inhibiting and reversing nonenzymatic cross-linking (protein ageing). However, the instant claims relate to reducing intraocular pressure or improving ocular accommodation by administering *a combination of a compound of formula I and a cholinergic agent*. There is no mention of any cholinergic agent in Cerami. There is no teaching or suggestion in Cerami of using a combination of the compounds of the invention (regardless of the nature of the counterion) with a cholinergic agent for reducing intraocular pressure or improving ocular accommodation. Therefore, Applicants respectfully request withdrawal of this rejection.

#### Administration

Claim 17 is rejected because “since Cerami discloses that administration may occur by other conventional means, it would have been obvious to one of ordinary skill in the art to further

modify the method of the prior art by administering the compounds intra-camerally because one of ordinary skill in the art would reasonably expect intra-cameral administration to effectively deliver the compounds to the eye.” Office Action at page 5.


As noted above, Cerami relates to thiazolium compositions and methods for inhibiting and reversing nonenzymatic cross-linking (protein aging). The instant claims relate to reducing intraocular pressure or improving ocular accommodation by administering *a combination of* a compound of formula I and a cholinergic agent. The compounds can be administered, for example, intravenously or intracamerally.

There is no mention of any cholinergic agent in Cerami. There is no teaching or suggestion in Cerami of using a combination of the compounds of the invention with a cholinergic agent (administered ocularly, topically, or otherwise) for reducing intraocular pressure or improving ocular accommodation. Therefore, Applicants respectfully request withdrawal of this rejection.

### CONCLUSION

On the basis of the foregoing amendment and remarks, Applicants respectfully submit that the pending claims are in condition for allowance and a Notice of Allowance for the pending claims is respectfully requested. If there are any questions regarding this application that can be handled in a phone conference with Applicants’ Attorneys, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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